

US EPA ARCHIVE DOCUMENT

Shaughnessy No.: 128857

Date out of ~~APR~~ 12 1988

To: Lois Rossi
Product Manager 21
Registration Division (TS 767C)

From: Emil Regelman, Supervisory Chemist
Review Section #3
Exposure Assessment Branch
Hazard Evaluation Division (TS 769C)

Thru: Paul F. Schuda, Chief
Exposure Assessment Branch/HED (TS 769C)

R

Paul F. Schuda

Attached, please find the EAB review of...

Reg./File #: 707-ERN, -ERR, -ERE, -ROG

Chemical Name: Myclobutanil aka Systhane

Type Product: fungicide

Product Name: RH-0611 WP Fungicide

Company Name: Rohm and Haas Company

Purpose: review of registrant's response to previous EAB
reviews

Date Received: 2/8/88

Action Code: 111, 126

Date Completed: APR 12 1988

EAB #(s): 80375, -76, -77, -78

80482, 80472

Monitoring Study Requested: ¹

Total Reviewing Time: 3.0 Days

Monitoring Study Volunteered:

Deferrals to: Ecological Effects Branch

Residue Chemistry Branch

Toxicology Branch

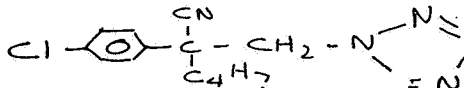
1. CHEMICAL:

chemical name: [alpha-butyl-alpha(4-chlorophenyl)-1H-1,2-triazole-1-propanenitrile

common name: Myclobutanil

trade name: Systhane, Rally

structure:



CAS #: 66871-89-0

Shaughnessy #: 128857

2. TEST MATERIAL: n.a.

3. STUDY/ACTION TYPE: response to EAB reviews

4. STUDY IDENTIFICATION:

Morelli, Michael A. Comments on the EPA/HED/EAB Reviews of Environmental Fate Studies. Rohm and Haas Company, Philadelphia, PA. received EPA 2/3/88 under rec. #s 214083, -84, -85, -86

Ackermann, I.B. Addendum to Aqueous Photolysis Study TR No. 31H-86-08. Rohm and Haas Company, Philadelphia, PA. Received EPA 2/25/88 under Acc. # 405-28801.

Stavinski, S.S. Reply to EAB Review of January 27, 1988 for Triazole Field Soil Accumulation Study and Triazole Storage Stability Study in Soil. Rohm and Haas Company, Philadelphia, PA. Received EPA 2/23/88 under Acc. # 405234-01.

5. REVIEWED BY:

Typed Name: E. Brinson Conerly
Title: Chemist, Review Section 3
Organization: EAB/HED/OPP

E.B. Conerly 4/12/88

6. APPROVED BY:

Typed Name: Emil Regelman
Title: Supervisory Chemist, Review Section 3
Organization: EAB/HED/OPP

Emil Regelman
APR 12 1988

7. CONCLUSIONS:

The status of the data requirements discussed below is as follows:

photolysis in water — acceptable, provided the applicant submits a satisfactory comparison of the intensity of the light source to natural sunlight. The compound is apparently stable to photolysis in water. Although there are serious deficiencies in the study, a careful examination indicates that it is likely that

no additional information would be gained by requiring the applicant to repeat the study using Guidelines conditions.

photolysis in soil — acceptable. The compound is stable to photolysis on soil, extrapolated half-life of ca. 143 days. Although there are serious deficiencies in this study also, it is likely that no further useful information would be gained by an additional study.

anaerobic soil metabolism — acceptable. The temperature at which it was performed has been supplied [the same temperature as the aerobic phase]. The compound is resistant to anaerobic metabolism — no detectable degradation after ca. 60 days.

leaching — additional data required re "aged" compound—degradates must be identified and quantified.

terrestrial field dissipation — unacceptable, due to inadequacy of sampling; to lack of immediate post-treatment sampling of the PA site (which means that application rate was not confirmed); a difference of almost an order of magnitude in soil concentration between the two sites, in what should have been comparable samples; and apparent difficulties with the analytical method.

fish bioaccumulation — waived, based on low k_{ow} s for parent and degradates. The compound is not expected to bioaccumulate.

8. RECOMMENDATIONS:

The applicant should supply the missing information with all due speed. Note that the characteristics of this compound, stability and mobility, mark it as a potential contaminator of ground-water.

9. BACKGROUND:

The applicant is attempting to complete full registration requirements for apples and grapes. The status of other data requirements follows:

hydrolysis — fulfilled, stable to hydrolysis

aerobic soil metabolism — fulfilled (JHJ 5/19/87) , half life of 60-70 days; at 367 days post treatment parent sythane comprised 29-33% of recovered radioactivity, with major degradates CO₂, 1,2,4-triazole, and beta-4-chlorophenyl-beta-cyano-gamma-(1H-1,2,4-triazole)-butyric acid

adsorption/desorption — fulfilled, unaged compound is of intermediate mobility in five soils

10. DISCUSSION OF INDIVIDUAL TESTS OR STUDIES:

10.1 A. Study Identification

Morelli, Michael A., Comments on the EPA/HED/EAB Reviews of Environmental Fate Studies. Rohm and Haas Company, Philadelphia, PA. received EPA 2/3/88 under rec. #s 214083, -84, -85, -86

E. Reviewer's Discussion and Interpretation of Study Results

photodegradation in water —

general comments

1) previous reviewer comment:

Results from TLC analyses... were presented as percent of recovered rather than percent of applied, and recoveries of radioactivity applied to the TLC plates were not reported.

Rohm and Haas response:

Radioactivity applied to the TLC plate was quantitatively recovered since the entire TLC channel was scraped and counted. For this reason, also, the % recovered recoveries should equal the % applied recoveries.

FAB reply:

This is a reasonable assumption, but should have been made explicit and obvious in the initial report. This deficiency can be considered resolved.

2) previous reviewer comment:

The incubation temperature was not $25 \pm 1^{\circ} \text{C}$

Rohm and Haas response:

Although the solution temperature in this study was slightly higher than recommended, the difference had no bearing on the outcome....This is borne out by the results for the dark control which showed the test compound was stable; no thermal degradation was observed.

FAB reply:

This deficiency is resolved.

3) previous reviewer comment:

The concentration of the cosolvent was not specified.

Rohm and Haas response:

The required information is provided....

EAB reply:

This deficiency is resolved. The concentration of the cosolvent was 0.2% (EBC 12/22/87).

4) previous reviewer comment:

The test solutions were not buffered.

Rohm and Haas response:

The hydrolysis study accepted by EAB shows test compound does not hydrolyze at environmental pH. Therefore, absence of buffer does not alter the result.

EAB reply:

This deficiency is resolved. The applicant is correct.

5) previous reviewer comment:

The registrant implied, but did not specify, that radioactivity applied to the C-18 column was quantitatively recovered.

Rohm and Haas response:

The report does not state explicitly the quantitative recovery of radioactivity...however, one can determine...it...by referring to the raw data in the Appendices.

EAB reply:

A reviewer is not expected to, and indeed should not, make inferences from raw data when the applicant has not made these same inferences. We accept the statement that recovery was essentially 100%. The applicant has submitted an addendum to the report detailing recoveries for that portion of the study. [See 10.2]

Study in Sterile, Deionized Water

1) previous reviewer comment:

There were no dark controls for triazole ring-labeled [¹⁴C] SYSTHANE.

Rohm and Haas response:

Guidelines state one or more concentrations should be used as dark control. Phenyl-labeled RH-3866 was used as the dark control. This is sufficient as location of the label has no bearing on chemical stability.

FAB reply:

The applicant appears to be correct. This deficiency is resolved.

2) previous reviewer comment:

The study was not conducted for 30 days or one half-life...

Rohm and Haas response:

Guidelines state the study irradiation conditions should be equivalent to 12 hours of light per day for 30 days. We have complied with this requirement by conducting the study for 15 days of continuous radiation.

FAB reply:

FAB cannot assess whether 15 days illumination with this light source is equivalent to 30 days natural sunlight, since the applicant has not provided us with a comparison of overall intensity of this light vs natural summer sunlight. This study will be acceptable if the applicant submits a satisfactory comparison.

3) previous reviewer comment:

The incubation temperature for the dark control was not reported.

Rohm and Haas response:

The temperature of all controls was the same and was reported.

FAB reply:

It is now our understanding that controls were maintained at ca. 31⁰ C, as were irradiated samples. This deficiency is resolved.

Study in Sterile, Deionized Water with Photosensitizer

1) previous reviewer comment:

There were no dark controls.

Rohm and Haas response:

Although a dark control with sensitizer is probably a good idea, the guidelines do not explicitly require it.

[It] requires only a dark control with water and we have complied with this requirement.

EAB reply:

The use of photosensitizers is not required. The study in question is therefore supplemental, and this deficiency does not affect the status of registration of the chemical.

2) previous reviewer comment:

TLC characterization of triazole ring-labeled [¹⁴C] SYSTHANE degradates (table 7 in text) was missing.

Rohm and Haas response:

We provide the missing Table 7 in the study supplement submitted with this response.

EAB reply:

See comment 1) above.

3) previous reviewer comment:

Quantitative data from TLC characterization of water eluates were not provided.

Rohm and Haas response:

The reviewer is correct. However, Figure 19 makes it quite clear that the vast majority of radioactivity reported in Table 4 for [¹⁴C] triazole label is, in fact, triazole. We do not believe this sole deficiency renders the study unacceptable for registration.

EAB reply:

See comment 1) above.

photodegradation in soil

Rohm and Haas:[not an exact quotation of the applicant's words]

The light source used in the previous experiment is adequate. The lack of photolability exhibited by the compound using this light source is also indicative of its photostability when subjected to natural light. One can extrapolate from the data that the compound has a half-life of ca 143 days.

EAB reply:

This specific deficiency is resolved. The data do indicate that the compound is stable when subjected to the experimental light conditions described, and the applicant presents a convincing rationale in this case for accepting the study. However, this is not intended to set a precedent for future studies by this applicant or others to deviate widely from Guidelines on experimental conditions.

aerobic and anaerobic soil metabolism

Rohm and Haas:[not an exact quotation of the applicant's words]

A previous review [JHJ 5/19/87, EAB # 70103] indicates that the aerobic soil metabolism study is acceptable. Sampling temperature provided (11/26/85) for the anaerobic study should now make this study acceptable.

EAB reply:

This information completes the anaerobic soil metabolism data requirement

soil column leaching

previous reviewer comment:

EAB notes that this study is scientifically valid, but does not fulfill guideline requirements. Soil residues not identified before or after leaching. Leachate degradates not completely identified and no k_d values reported.

Rohm and Haas:

This study is one of several we cite to satisfy the mobility requirement for full registration. EAB has accepted fully the adsorption/desorption study...and accepted conditionally the aged-soil column study... That condition....was that we provide leaching data on aged free triazole. Therefore, the triazole-aged residue column study...was intended as a supplementary study. Inasmuch as EAB accepts that the study is scientifically valid, we believe we have complied with EAB's request to provide leaching data on triazole. For this reason, it is incorrect to conclude we had not fulfilled the mobility requirement for full registration just because the study is non-guideline. In our judgement, the two soil column studies together fulfill the data requirement.

EAB reply:

The objections expressed by the previous reviewer were not limited to those noted in the above "previous reviewer's comment", but included uncertainty as to the length of time taken for the elution, which could have been as much as a month, allowing further degradation to occur. Since the radiolabel is distributed almost equally between leachate and soil column, and ca. 25% remains in the topmost layer, several entities are obviously present, and have not been identified. The report is not complete without this information.

terrestrial field dissipation

In addition to the comments below, we note that in the PA site, the first sample taken after day 0 was at day 24, when only ca 20% of the initial material remained.

1) previous reviewer comment:

Pretreatment samples were not taken at either test site.

Rohm and Haas response:

Pretreatment soil samples were analyzed at each site. Samples contained 0.0 ppm residue. Results appear in Appendix I, p. 18, Sample No. 001 for soil from Cleveland, MS and in Appendix II, p. 164, Sample No. 001 for soil from Newtown, PA.

EAB reply:

This deficiency is resolved by this statement from the applicant.

2) previous reviewer comment:

At the PA site, immediate posttreatment samples were not taken following the initial application.

Rohm and Haas response:

This is an oversight on our part. Field personnel did not take posttreatment samples at PA site, but did at MS site. The absence of data, however, does not affect the scientific validity of the half-life value under field conditions.

EAB reply:

The immediate post-treatment samples serve to confirm the application rate and degree of uniformity of application. The lack of these data is a serious

deficiency in the study. This deficiency is not resolved.

3) previous reviewer comment:

No explanation was provided for the difference in the 0 day concentrations of the test substance found at the two sites.

Rohm and Haas response:

Difference may be attributed to inhomogeneous sampling at PA site and different crop densities at two locations at the time of application. Scientific conclusion regarding dissipation rates is unaltered by observed differences in 0 day concentrations.

EAB reply:

The explanation offered by the applicant may be valid, but can only be speculative at this point. The observed difference in day 0 concentrations may reflect a real difference in application rate, and it is not necessarily true that dissipation rates are unaffected by initial application rate. For instance, the adsorptive capacity of the soil could have been exceeded in one case and not in the other, which could result in very different apparent dissipation rates in the two soils. Further, the applicant indicates that there was an apparent problem in sampling ["inhomogeneous sampling at PA site"] which casts further doubt on the analytical results. Both the applicant and EAB will be better served by submission of a new study containing complete and reliable information.

4) previous reviewer comment:

Field test data including depth to water table, slope of the test site and soil temperatures were not reported.

Rohm and Haas response:

The required information on depth to water table and slope of test site is provided in the study supplement submitted with this response. Soil temperatures were not measured, but we have now established appropriate monitoring stations on site to satisfy this data requirement for future studies.

EAB reply:

Proper monitoring of future studies cannot retroactively repair this study. This deficiency and the others mentioned above make this study unacceptable.

5) previous reviewer comment:

Degradates were not characterized.

Rohm and Haas response:

We already satisfied this requirement by submitting an addendum to the field dissipation study... entitled "Triazole Field Soil Accumulation Study" (Acc. No. 265750)... EAB should expedite review of this study.

EAB reply:

This study has been reviewed (EBC 1/27/88), and was found unacceptable. [See also 10.3.]

fish bioaccumulation

Rohm and Haas response:

EAB reviews granted a waiver of this study based on K_{OWS} for parent and metabolites.

EAB reply:

The applicant is correct. [See JHJ 5/19/87.]

10.2 A. Study Identification

Ackermann, I.B. Addendum to Aqueous Photolysis Study TR No. 31H-86-08. Rohm and Haas Company, Philadelphia, PA. Received EPA 2/25/88 under Acc. # 405-28801.

B. Materials and Methods: n.a.

C. Reported Results: attached

D. Study Author's Conclusions:

Percentage recoveries ranged from 92 to 114% over the C₁₈ sep-pak columns.

E. Reviewer's Discussion and Interpretation of Study Results

The applicant has provided the necessary documentation of the recoveries as required in 10.1 above.

10.3 A. Study Identification

Stavinski, S.S. Reply to EAB Review of January 27, 1988 for Triazole Field Soil Accumulation Study and Triazole Storage Stability Study in Soil. Rohm and Haas Company, Philadelphia, PA. Received EPA 2/23/88 under Acc. # 405234-01.

E. Discussion and Interpretation of Study Results

1) previous reviewer comment:

Analytical precision appears to be unacceptable. Results cannot be explained by smaller spikes giving poorer recovery.

Rohm and Haas response:

We believe the study to be scientifically valid and guideline. The increased variability (unacceptable precision) referred to in fortification results arises from background levels of triazole in control soil at the two study locations and does not reflect the analytical precision for analysis of treated samples. This is an expected result for any analytical method where the field controls contain natural background levels of the analyte. Control soils that were fortified contained naturally occurring levels of triazole ranging from 0.0005 ppm (method sensitivity) to 0.018 ppm. This introduces the increased variability in fortifications, especially low level fortifications because residues found in the fortified sample are corrected for residues present before fortification in the control. At lower levels of fortification two numbers close in magnitude are subtracted which leads to an increase in the variability of the method accuracy of the analysis. Treated samples are not corrected for the control corrections which introduces the increased variance, therefore, their residue levels reflect the true variance (precision) of the analytical method. If this is true, low level fortifications would have the same average recovery (reflects accuracy of analysis) as high level fortifications but would show increased variability (precision) over the normal analytical method precision. The result of analyses of treated samples would not be affected.

This is proven by the analytical data. Fortification results are summarized below. [attached]

FAB reply:

The new figures the applicant presents indicate roughly the same average recovery for the two (high vs low) sets of results. However the average variability in the low level spiked samples is 26%, vs 11 % for the high samples. This seems to indicate that precision is indeed influenced by spike size. 6/18 (1/3) recovery values are less than 70% in the set of lower values, and 4/21 (1/5) in the set of higher values. Lower analytical values (below 0.05 ppm) are, by inference from these data, less reliable.

2) previous reviewer comment:

Only mean values are reported for analyzed samples. We do not know whether the variability between replicates may be as great as that reported in the analyses of fortified samples.

Rohm and Haas response:

Further proof of the validity of the analytical data is provided by the results of analyses for duplicate and replicate samples. Contrary to ...the review that only mean values are reported, all individual analytical determinations for every treated sample are reported in Appendices 1 and 2, Detailed Residue Data. All raw data in this report was fully audited during the recent EPA audit at Rohm and Haas.

Duplicate samples are defined as the same soil sample analyzed repeatedly. They provide a true measure of the precision of the analytical method. The data are shown below. [Attached]

Replicate samples, which measure the precision of all aspects of the entire study, show an excellent precision. The average standard deviation is only 0.010 ppm between replicate samples. This is outstanding for a large scale field soil dissipation study. [Values attached]

EAB reply:

Some of the repeatedly analyzed samples show good agreement, but 3/8 show approximately 100% variation between samples. This can hardly be considered good agreement.

8/12 of the replicate values (different soil samples taken on the same day) are approximately the same as the reported standard deviation, or smaller. This results in an unacceptable uncertainty in these values.

3) previous reviewer comment

storage stability study — The behavior of the compound may be as described, but, as in the field dissipation study, the analytical results are so erratic (two-fold variation in nominal replicates) that they do not support this conclusion.

Rohm and Haas response

We strongly disagree that the analytical results are erratic. We believe the analytical results support the study conclusion and that the study is valid. [Values attached.] The average standard deviation is $\pm 8.7\%$, which clearly indicates the analytical results are valid and support the study conclusions.

EAB reply

To average these "standard deviations" would be no more valid than to report a mean recovery value based on all the samples analyzed. Moreover, there are too few analyses in each treatment set (except for the freshly fortified set) for a standard deviation to be significant. Two sets of analyses, the fresh and 99 day R.T. are apparently in good agreement. Two others, the 35 day R.T. and 35 day frozen are acceptable. The 9 day R.T. and 99 day frozen are unacceptably deviant, "replicate" samples varying by almost 100%.

11. COMPLETION OF ONE-LINER: n.a.
12. CBI APPENDIX: attached

Myclobutanil environmental fate review

Page _____ is not included in this copy.

Pages 15 through 19 are not included in this copy.

The material not included contains the following type of information:

- ☐ Identity of product inert ingredients
 - ☐ Identity of product impurities
 - ☐ Description of the product manufacturing process
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